An Analysis of Cumulative Risks Indicated by Biomonitoring Data of Six Phthalates Using the Maximum Cumulative Ratio

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The Maximum Cumulative Ratio (MCR) quantifies the degree to which a single component of a chemical mixture drives the cumulative risk of a receptor.[ADDIN CSL_CITATION { "citationItems" : [{ "id" : "ITEM-1", "itemData" : { "DOI" : "10.3390/ijerph8062212", "ISBN" : "1660-4601", "ISSN" : "16604601", "PMID" : "21776227", "abstract" : "Due to the vast number of possible combinations of chemicals to which individuals are exposed and the resource-intensive nature of cumulative risk assessments, there is a need to determine when cumulative assessments are most required. This paper proposes the use of the maximum cumulative ratio (MCR) as a tool for this evaluation. MCR is the ratio of the cumulative toxicity received by an individual from exposure to multiple chemical stressors to the largest toxicity from a single chemical stressor. The MCR is a quantitative measure of the difference in an individual's toxicity estimated using a chemical-by-chemical approach and using an additive model of toxicity. As such, it provides a conservative estimate of the degree to which individuals' toxicities could be underestimated by not performing a cumulative risk assessment. In an example application, MCR is shown to be applicable to the evaluation of cumulative exposures involving up to 81 compounds and to provide key insights into the cumulative effects posed by exposures to multiple chemicals. In this example, MCR values suggest that individuals exposed to combinations of chemicals with the largest Hazard Indices were dominated by the contributions of one or two compounds.", "author" : [{ "dropping-particle" : "", "family" : "Price", "given" : "Paul S.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Han", "given" : "Xianglu", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }], "container-title" : "International Journal of Environmental Research and Public Health", "id" : "ITEM-1", "issue" : "6", "issued" : { "date-parts" : [["2011"]] }, "page" : "2212-2225", "title" : "Maximum cumulative ratio (MCR) as a tool for assessing the value of performing a cumulative risk assessment", "type" : "article-journal", "volume" : "8" }, "uris" : ["http://www.mendeley.com/documents/?uuid=e0ca9bb7-517b-445c-9a10-b9dc1d270fe2"] }], "mendeley" : { "formattedCitation" : "¹", "plainTextFormattedCitation" : "1", "previouslyFormattedCitation" : "¹" }, "properties" : { "noteIndex" : 0 }, "schema" : "https://github.com/citation-style-language/schema/raw/master/csl-citation.json" }] This study used the MCR, the Hazard Index (HI) and Hazard Quotient (HQ) to evaluate co-exposures to six phthalates using biomonitoring data in 2454 individuals aged 6 years and older from the 2011-12 cycle of the National Health and Nutrition Examination Survey. The values of MCR, HI and phthalate-specific HQs were determined by calculating steady-state doses consistent with the concentrations of phthalate metabolites in urine and using Tolerable Daily Intake values.[ADDIN CSL_CITATION { "citationItems" : [{ "id" : "ITEM-1", "itemData" : { "DOI" : "10.1016/j.yrtph.2014.04.019", "ISSN" : "10960295", "PMID" : "24815596", "abstract" : "Exposures to multiple chemicals may contribute to increased risk of similar adverse effects. Cumulative risk may be estimated using a hazard index (HI), the sum of individual hazard quotients (HQ, ratio of exposure to the reference value). We demonstrate the HI approach for five phthalates: di(2-ethylhexyl) phthalate (DEHP), di-n-butyl phthalate (DBP), diisobutyl phthalate (DiBP), diisononyl phthalate (DiNP), and butyl benzyl phthalate (BBP). Phthalate exposure for the US

general population is estimated using urine metabolite levels from NHANES, extrapolating to ingested 'dose' using the creatinine correction approach. We used two sets of reference values: European Union Tolerable Daily Intakes and Denmark Environmental Protection Agency Derived No Effect Levels. We also investigated the use of an alternate reference value for DEHP, derived from a recent study on male reproductive system development. HQs and HIs were calculated for the total population ages 6. years and older, as well as for men and women of approximate reproductive age (18-39. years), and children (6-11. years). Median HQs ranged from <0.01 for BBP, to ~0.1 (using established values) or ~2 (using an alternate value) for DEHP. Median HIs were <0.30 (95th percentiles just > 1.0), and were driven by DEHP and DBP exposures. ?? 2014.", "author" : [{ "dropping-particle" : "", "family" : "Christensen", "given" : "Krista L Y", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Makris", "given" : "Susan L.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Lorber", "given" : "Matthew", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }], "container-title" : "Regulatory Toxicology and Pharmacology", "id" : "ITEM-1", "issue" : "3", "issued" : { "date-parts" : [["2014"]] }, "page" : "380-389", "publisher" : "Elsevier Inc.", "title" : "Generation of hazard indices for cumulative exposure to phthalates for use in cumulative risk assessment", "type" : "article-journal", "volume" : "69" }, "uris" : ["http://www.mendeley.com/documents/?uuid=aab6a7b4-0ebc-4b3d-b1e7-c61e39c01d75"] }], "mendeley" : { "formattedCitation" : "²", "plainTextFormattedCitation" : "2", "previouslyFormattedCitation" : "²" }, "properties" : { "noteIndex" : 0 }, "schema" : "https://github.com/citation-style-language/schema/raw/master/csl-citation.json" }] There were 22 individuals (0.9%) predicted to have at least one HQ value > 1 and an additional 17 (0.7%) with no HQ value > 1 but with an HI value > 1. The percent of individuals with HI values > 1 differed by age (0.9% for individuals between 6 – 17 y and 1.9% for individuals > 17 y). There is a statistically significant negative relationship between HI and MCR values in both age groups (p-value < 0.001). This relationship indicates that individuals with the largest HI values tend to receive them from exposures to one phthalate rather than from combined exposures to multiple phthalates. Confirming this finding, the average (range) of HI values for individuals with an HI > 1 and all HQs < 1 and individuals with at least one HQ > 1 were 1.1 (1.0-1.3) and 2.8 (1.1-13.7), respectively. The combined assessment found that 17/39 (43%) of the individuals with HI values > 1 are missed by chemical-by-chemical assessments of the phthalates. These findings suggest that determining combined exposures for the six phthalates has a modest impact on the predictions of the chemicals' risks. Additional individuals with HI values >1 are identified, but HI values in these individuals are close to 1 (<1.3). Individuals with the largest HI values are identified by chemical-by-chemical assessments. The views expressed in this abstract are those of the authors and do not necessarily reflect the views or policies of the U.S. EPA.

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